510,088

Translation

PCT/JP2003/014263

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY
(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70) Rec'd PCT/PTO 15 AUG 2005

Applicant's or agent's file reference FP148OP1618	FOR FURTHER ACTION	See Form PCT/IPEA/416
International application No. PCT/JP2003/014263	International filing date (*day/month/year*) 10 November 2003 (10.11.2003)	Priority date (*day/month/year*) 29 November 2002 (29.11.2002)
International Patent Classification (IPC) or national classification and IPC A61K 38/57, A61P 1/02, 3/14, 19/10, 31/04, 31/12, 35/00, 43/00		
Applicant MORINAGA MILK INDUSTRY CO., LTD.		

1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 10 sheets, including this cover sheet.

3. This report is also accompanied by ANNEXES, comprising:

   a. ☐ *(sent to the applicant and to the International Bureau)* a total of _____ sheets, as follows:

      ☐ sheets of the description, claims and/or drawings which have been amended and are the basis of this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).

      ☐ sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.

   b. ☒ *(sent to the International Bureau only)* a total of (indicate type and number of electronic carrier(s)) comprising 1 flexible disk, containing a sequence listing and/or tables related thereto, in computer readable form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).

4. This report contains indications relating to the following items:

- ☒ Box No. I Basis of the report
- ☐ Box No. II Priority
- ☒ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☒ Box No. VIII Certain observations on the international application

Date of submission of the demand 16 February 2004 (16.02.2004)	Date of completion of this report 15 July 2004 (15.07.2004)
Name and mailing address of the IPEA/JP Facsimile No.	Authorized officer Telephone No.

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
PCT/JP2003/014263

Box No. I Basis of the report

1. With regard to the language, this report is based on the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ This report is based on translations from the original language into the following language _____, which is language of a translation furnished for the purpose of:

☐ international search (under Rules 12.3 and 23.1(b))

☐ publication of the international application (under Rule 12.4)

☐ international preliminary examination (under Rules 55.2 and/or 55.3)

2. With regard to the **elements** of the international application, this report is based on *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report)*:

☒ The international application as originally filed/furnished

☐ the description:

pages _____, as originally filed/furnished

pages* _____ received by this Authority on _____

pages* _____ received by this Authority on _____

☐ the claims:

pages _____, as originally filed/furnished

pages* _____, as amended (together with any statement) under Article 19

pages* _____ received by this Authority on _____

pages* _____ received by this Authority on _____

☐ the drawings:

pages _____, as originally filed/furnished

pages* _____ received by this Authority on _____

pages* _____ received by this Authority on _____

☐ a sequence listing and/or any related table(s) – see Supplemental Box Relating to Sequence Listing.

3. ☐ The amendments have resulted in the cancellation of:

☐ the description, pages _____

☐ the claims, Nos. _____

☐ the drawings, sheets/figs _____

☐ the sequence listing *(specify)*: _____

☐ any table(s) related to sequence listing *(specify)*: _____

4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).

☐ the description, pages _____

☐ the claims, Nos. _____

☐ the drawings, sheets/figs _____

☐ the sequence listing *(specify)*: _____

☐ any table(s) related to sequence listing *(specify)*: _____

* *If item 4 applies, some or all of those sheets may be marked "superseded."*

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
PCT/JP2003/014263

Supplemental Box Relating to Sequence Listing

Continuation of Box No. 1, item 2:

1. With regard to any nucleotide and/or amino acid sequence disclosed in the international application and necessary to the claimed invention, this report was established on the basis that of:

   a. type of material

   ☒ a sequence listing

   ☐ table(s) related to the sequence listing

   b. format of material

   ☐ in written format

   ☒ in computer readable form

   c. time of filing/furnishing

   ☐ contained in the international application as filed

   ☒ filed together with the international application in computer readable form

   ☐ furnished subsequently to this Authority for the purpose of search and/or examination

   ☐ received by this Authority as an amendment* on _____

2. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table(s) relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

3. Additional comments:

** If item 4 in Box No. I applies, the listing and /or table(s) related thereto, which form part of the basis of the report, may be marked "superseded".*

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
PCT/JP2003/014263

Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application.

☒ claims Nos. 13

because:

☒ the said international application, or the said claims Nos. 13 relate to the following subject matter which does not require an international preliminary examination *(specify)*:

See supplemental sheet

☐ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. _____ are so unclear that no meaningful opinion could be formed *(specify)*:

☐ the claims, or said claims Nos. _____ are so inadequately supported by the description that no meaningful opinion could be formed.

☒ no international search report has been established for said claims Nos. 13 .

☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:

the written form
- ☐ has not been furnished
- ☐ does not comply with the standard

the computer readable form
- ☐ has not been furnished
- ☐ does not comply with the standard

☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions.

☐ see Supplemental Box for further details.

Supplemental Box
(To be used when the space in any of the preceding boxes is not sufficient)

Continuation of: III.1

The invention that is set forth in claim 13 pertains to a method for the treatment of the human body by therapy (PCT Article 34(4)(a)(i) and PCT Rule 67.1(iv)).

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.
PCT/JP 03/14263

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims	3, 4, 10-12, 16, 17, 23, 24	YES
	Claims	1, 2, 5-9, 14, 15, 18-22	NO
Inventive step (IS)	Claims	3, 4, 16, 17	YES
	Claims	1, 2, 5-12, 14, 15, 18-24	NO
Industrial applicability (IA)	Claims	1-12, 14-24	YES
	Claims		NO

2. Citations and explanations

The present written opinion is drafted on the basis of the disclosures of the following documents, which are cited in the international search report.

Document 1: H. S. LEE, K. J. LEE, Peptides, 2000, 21, pages 807 to 809

Document 2: EP 679659 A1 (Taiho Pharmaceutical Co., Ltd.)

Document 3: JP 7-242600 A (Yoshimitsu NAGAO)

Document 4: JP 9-221425 A (Taiho Pharmaceutical Co., Ltd.)

Document 5: WO 98/49152 A1 (Smithkline Beecham Corp.)

Document 6: JP 2001-139534 A (Yoshimitsu NAGAO)

Document 7: JP 2000-72797 A (Taiho Pharmaceutical Co., Ltd.)

Document 8: EP 822260 A1 (Taiho Pharmaceutical Co., Ltd.)

Document 9: JP 7-2896 A (Snow Brand Milk Products Co., Ltd.)

Document 10: JP 7-126294 A (Snow Brand Milk Products Co., Ltd.)

Document 11: Y. MATSUOKA et al., Biosci. Biotechnol. Biochem., 2002, 66 (12), pp. 2531 to 2536

Document 12: Beta casein precursor, [online], SWISS-PROT,

1988, [retrieved on 12 December 2003], retrieved from JPO DNA Database, Accession No. PO5814

Claims 1, 2, 5 to 9, 14, 15 and 18 to 22

Document 1 indicates that the peptide product which results from the hydrolysis of bovine β-casein by means of pancreatic fluid exhibits a cathepsin B-inhibiting action, and presents the specific peptide sequence thereof. Therein, a comparison of the inventions that are set forth in claims 1, 2, 5 to 9, 14, 15 and 18 to 22 and the invention that is indicated in document 1 shows that the former inventions delimit the specific degree of hydrolysis to which the hydrolysis products are subjected, delimit the specific content of the hydrolysis products within the compositions and present the sequence of the peptide as expressed in humans; therefore, the former inventions include portions that differ from the latter inventions.

However, the features of delimiting the degree of hydrolysis to which the hydrolysis products are subjected and of delimiting the content of the hydrolysis products are considered to be common knowledge to a person skilled in the art of the technical field related to compositions which include hydrolysis products, and as such can be configured in an arbitrary and appropriate manner. In addition, the sequence of the peptide as expressed in humans is well known, as presented in document 12; therefore, it is not considered to require any significant creativity for a person skilled in the art to attempt to substitute the human peptide sequence for the bovine peptide sequence.

Consequently, the inventions that are set forth in claims 1, 2, 5 to 9, 14, 15 and 18 to 22 lack novelty and do not involve an inventive step in the light of the

disclosures of documents 1 and 12.

Claims 10 to 12, 23 and 24

The inventions that are set forth in claims 10 to 12, 23 and 24 employ cysteine protease inhibitors for the prevention or treatment of diseases; therefore, the inventions in question differ from the inventions that are indicated in documents 1 and 12.

However, diseases that are induced by cathepsin as well as the prevention or treatment of the diseases in question via the administration of a cathepsin inhibitor are disclosed in documents 2 to 11; therefore, these items are considered to be well known to a person skilled in the art. As a result, it cannot be said to be especially difficult for a person skilled in the art to conceive of using the peptides that are presented in documents 1 and 12 for the prevention or treatment of the various diseases that are disclosed in documents 2 to 11.

Consequently, the inventions that are set forth in claims 10 to 12, 23 and 24 do not involve an inventive step in the light of the disclosures of documents 1 to 12.

Claims 3, 4, 16 and 17

The inventions that are set forth in claims 3, 4, 16 and 17 delimit the specific amino acid sequence of the peptide which serves as the active component of the cysteine protease inhibitors.

Therein, the prior art that is presented in relation to the specific sequence for the casein is not cited in the international search report; therefore, it cannot be said to be easy for even a person skilled in the art to conceive of the inventions that are set forth in claims 3, 4, 16 and 17 in the light of the disclosures of the documents in question.

Consequently, the inventions that are set forth in

claims 3, 4, 16 and 17 are novel and involve an inventive step in relation to the disclosures of documents 1 to 12.

VIII. Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

Claims 1 to 12 and 14 to 24

The inventions that are set forth in the present application are characterized by the technical feature wherein casein, a partial peptide from casein and/or a hydrolysis product from casein exhibit a cysteine protease inhibiting activity.

However, the document JP 5-184382 A (Kyodo Nyugyo Kabushiki Kaisha) indicates that αs-, β-, and κ- casein exhibit a cysteine protease-inhibiting activity of 0%. In addition, the document J. SUZUKI, N. KATOH, (Jpn. J. Vet. Sci., 1990, 52 (5), pp. 947-954) indicates that cysteine proteases hydrolyse casein; therefore, the document in question is considered to disclose a feature which contradicts the technical characteristic of the inventions that are set forth in the present application.